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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/011,797	07/23/1998	MARC PARMENTIER	VANMA72.001A	1370

7590 10/07/2003

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	30

DATE MAILED: 10/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/011,797	PARMENTIER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/17/2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,37,38,40-42,47 and 59-65* is/are pending in the application.

4a) Of the above claim(s) *61-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,37,38,40-42,47,59 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 35, 37-38, 40-42, 47, 59-65 are pending. Claims 61-65 are withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention. The method of identifying an agonist of antagonist of the ORL1 receptor using SEQ ID NO: 2 and the peptides and nucleic acids of the claims under consideration are drawn to separate, distinct inventions and are distinguished from each other because the special technical features which define them by chemical and physical characteristics i.e. structure/function, as well as biological functions are different and these special technical features are not shared by each invention. Since these special technical features are not shared by each product and since the common features do not establish an advance over the prior art (as set forth in the rejection under 35 USC 102(e), *infra*), the Groups do not form a single inventive concept within the meaning of Rule 13.2.

Claims 35, 37-38, 40-42, 47, 59-60 are under consideration.

Response to Arguments

Applicant's arguments filed in Paper No. 29, 7/17/2003 have been fully considered but they are not persuasive, for the reasons set forth below.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 37-38, 40-42, 47, 59, 60 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an amino acid of SEQ ID NO: 2-4, or a nucleic acid consisting of the sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for a nucleic acid which comprises nucleic acid sequences which encode SEQ ID NO: 2-4, or a nucleic acid molecule which comprises SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 35, 37-38, 40-42, 47, 59, 60 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of a ligand of ORL1. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of the ligands of ORL1. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals,

erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass variant nucleic acids and polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims as written do not set forth a functional limitation for the polynucleotides and the encoded polypeptides encompassed by the claims. Since the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polynucleotides and encoded polypeptides, since the skilled artisan would have to first make polypeptide variants, but there is no functional limitation set forth for the claimed encoded polypeptides. Thus, since Applicant has only taught how to test for polynucleotide and polypeptide variants of ORL1

ligands, and has not taught how to make polynucleotide and polypeptide variants of ORL1 ligands, it would require undue experimentation of one of skill in the art to make and use the claimed method.

Claims 35, 37-38, 40-42, 47, 59, 60 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a nucleic acid which comprises nucleic acid sequences which encode SEQ ID NO: 2-4, or a nucleic acid molecule which comprises SEQ ID NO: 1. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded SEQ ID NO: 2-4. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes

identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 1, and the polypeptide of SEQ ID NO: 2-4 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 35, 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene (1991).

The Stratagene catalogue teaches the use of random 9-mers capable of hybridizing to all gene sequences. The random primers meet the limitations of claims 35 and 37 in that said primers are isolated DNA which are complementary to a sequence as set forth in SEQ ID NO: 1.

Claim 60 is rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,837,809 (Grandy et al. 1998). U.S. Patent No. 5,837,809 has a priority date of Aug. 11, 1995.

Grandy et al. discloses ligands for a mammalian opioid receptor. One of the ligands disclosed as SEQ ID NO: 5 by Grandy et al. is 100% identical to the polypeptide with an amino acid sequence set forth in SEQ ID NO: 2 (see Sequence Comparison A, attached to Paper No. 8, 3/29/2000; also see column 18, lines 51-53), thus claim 60 is anticipated.

Applicant argues that the '809 patent is not prior art, and has submitted a Declaration under 37 CFR 1.132 to establishes prior conception and reduction to practice. However, this is insufficient to overcome the rejection, see 37 CFR 1.608, MPEP 2308.01, if the effective filing date of the application is 3 months or less after the effective filing date of the patent, the applicant must submit a statement alleging that there is a basis upon which the applicant is entitled to a judgment relative to the patentee. 37 CFR 1.608(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 40, 47, 59 stand rejected, and new claim 60 is rejected, under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,837,809 (Grandy et al. 1998). U.S. Patent No. 5,837,809 has a priority date of Aug. 11, 1995.

Grandy et al. discloses ligands for a mammalian opioid receptor. One of the ligands disclosed as SEQ ID NO: 5 by Grandy et al. is 100% identical to the polypeptide with an amino acid sequence set forth in SEQ ID NO: 2 (see Sequence Comparison A; also see column 18, lines 51-53). Grandy et al. discloses that the peptide can be produced by molecular or genetic engineering means (column 9, lines 27-28). Transformed host cells comprising vectors encoding the protein are disclosed at column 10, lines 45-50. Thus it would have been obvious to one of skill in the art at the time the invention to make a nucleic acid encoding the peptide of SEQ ID NO: 2. The motivation is provided at column 10, line 65 to column 11 line 13 which teaches that The recombinant expression constructs of the present invention are useful to transform cells which do not ordinarily express an opioid receptor to thereafter express the receptor. Such cells are useful as intermediates for making cell membrane preparations useful for receptor binding activity assays, which are in turn useful for drug screening. The recombinant expression constructs of the present invention thus provide a method for obtaining reagents for screening potentially useful drugs at advantageously lower cost than conventional animal screening protocols.

Applicant argues that the '809 patent is not prior art, and has submitted a Declaration under 37 CFR 1.132 to establishes prior conception and reduction to practice. However, this is insufficient to overcome the rejection, see 37 CFR 1.608, MPEP 2308.01, if the effective filing date of the application is 3 months or less after the effective filing date of the patent, the applicant must submit a statement alleging that there is a basis upon which the applicant is entitled to a judgment relative to the patentee. 37 CFR 1.608(a).

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
October 3, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600